Annals of Medicine and Surgery 63 (2021) 102141

Contents lists available at ScienceDirect

Annals of Medicine and Surgery

journal homepage: www.elsevier.com/locate/amsu

Cohort Study

Prevalence and risk factors of barotrauma in Covid-19 patients admitted to an intensive care unit in Kuwait; a retrospective cohort study

Hussein Elsaaran [a,1], Shamlan AlQinai [a,1], Dana AlTarrah [b,1], Mahdi Abdulrasoul [a], Sarah Al-Youha [a], Sulaiman Almazeedi [a], Mohannad Al-Haddad [a], Mohammad H. Jamal [a], Salman Al-Sabah [a,*]

[a] COVID-19 Research Team, Jaber Al-Ahmad Hospital, Kuwait
[b] Faculty of Public Health, Kuwait University, Kuwait

ARTICLE INFO

Keywords:
Barotrauma
Pneumothorax
COVID-19

ABSTRACT

Background: The development of barotrauma has been suggested to complicate the management of mechanically ventilated COVID-19 patients admitted to the intensive care unit (ICU). This study aims to identify potential risk factors associated with the development of barotrauma related complications in COVID-19 patients receiving mechanical ventilation.

Methods: A retrospective cohort study was carried out in a single COVID-19 designated center in Kuwait. Three hundred and forty-three confirmed COVID-19 patients transferred and/or admitted to our institution between February 26, 2020 and June 20, 2020 were included in the study. All patients were admitted into the ICU with the majority being mechanically ventilated (81.3%).

Results: Fifty-four (15.4%) patients developed barotrauma, of which 49 (90.7%) presented with pneumothorax, and 14.8% and 3.7% due to pneumomediastinum and pneumopericardium respectively. Of those that developed barotrauma, 52 (96.3%) patients were in acute respiratory distress syndrome (ARDS). Biochemically, the white blood cells ($p = 0.001$), neutrophil percentage ($p = 0.012$), lymphocyte percentage ($p = 0.014$), neutrophil: lymphocyte ratio (NLR) ($p=<0.001$) and lactate dehydrogenase (LDH) ($p = 0.002$) were found to be significantly different in patients that developed barotrauma. Intubation due to low level of consciousness ($p = 0.007$), a high admission COVID-GRAM score ($p = 0.042$), and a positive-end expiratory pressure (PEEP) higher than the control group ($p = 0.016$) were identified as potential risk factors for the development of barotrauma.

Conclusion: Patients infected with COVID-19 have a significant risk of developing barotrauma when receiving invasive mechanical ventilation. This poses a substantial impact on the hospital course of the patients and clinical outcome, correlating to a higher mortality rate in this cohort of patients.

1. Introduction

The novel coronavirus (COVID-19) has become a global pandemic [1]. This highly transmissible and infectious disease is found to affect multiple systems, particularly the respiratory tract. The prevalence of pneumothorax among COVID-19 patients in the intensive care unit (ICU) has been reported to be 2% [1,2]. More recently, studies have found that barotrauma-related complications due to invasive mechanical ventilation is increasingly reported, as incidence in COVID-19 patients was reported to be as high as 15% [3].

The association of acute respiratory distress syndrome (ARDS) and the development of secondary pneumothorax in mechanically ventilated patients is well documented as an independent risk factor of mortality [4–6]. The majority of patients that contract COVID-19 experience symptoms of a mild upper respiratory tract infection [7–9], however a small proportion of patients are found to develop severe pneumonia and sepsis with the potential development of ARDS and multi-system organ failure [9–12]. The development of ARDS and its associated

* Corresponding author.
E-mail addresses: Drhussein83@gmail.com (H. Elsaaran), s.albader.md@gmail.com (S. AlQinai), danah.altarrah@ku.edu.kw (D. AlTarrah), mabdulrasoul26@hotmail.com (M. Abdulrasoul), sarahalyouha@gmail.com (S. Al-Youha), smazeedi@gmail.com (S. Almazeedi), dr.moq8@hotmail.co.uk (M. Al-Haddad), mjamal110@gmail.com (M.H. Jamal), salman.k.alsabah@gmail.com (S. Al-Sabah).
[1] These authors contributed equally to the protocol, data collection, statistical analysis, and writing.

https://doi.org/10.1016/j.amsu.2021.01.089
Received 28 December 2020; Received in revised form 24 January 2021; Accepted 26 January 2021
Available online 5 February 2021

complications, which include septic shock, thrombotic complications, acute kidney injury (AKI), derangement of liver enzymes, cardiac injury and barotrauma are associated with poor clinical outcomes in COVID-19 patients [9–11]. There are a limited number of studies that have focused on the epidemiology and the potential risk factors associated with developing barotrauma in COVID-19 patients [11–13].

In our single-center study we aimed to identify clinical features and risk factors associated with the potential development of barotrauma in mechanically ventilated COVID-19 patients. The study also aims to investigate the impact in terms of clinical course and prognosis of COVID-19 when barotrauma related complications occur.

2. Methods

2.1. Study design and data collection

The present retrospective study included the first 343 confirmed COVID-19 patients transferred and/or admitted to our institution between February 26, 2020 and June 20, 2020. Our institution, located in the State of Kuwait, was dedicated solely to COVID-19 patients, predominantly for patients who were deemed critical and may require further support in the form of extracorporeal membrane oxygenation (ECMO) in the ICU.

Inclusion criteria were patients of all ages diagnosed with COVID-19 using PCR testing, in accordance with the World Health Organization (WHO) interim guidance. COVID-GRAM predictive risk score developed and internally validated in China was used to predict the risk of critical illness in hospitalized COVID-19 patients [14]. Ten variables at admission were used to predict critical illness. These include age, unconsciousness, hemoptysis, dyspnea, number of comorbidities, cancer history, chest X-ray abnormality, neutrophil to lymphocyte ratio, lactate dehydrogenase and direct bilirubin. The risk of developing critical illness was further categorized into three categories: low, medium and high.

All related patient information and clinical data were retrieved from the hospitals electronic medical record system. These included socio-demographic factors (age, gender, nationality), clinical indicators (unconsciousness on admission i.e. Glasgow coma score of less than 8, hemoptysis and shortness of breath) and biochemical inflammatory markers (white blood count, neutrophil percentage, lymphocyte percentage, neutrophil: lymphocyte ratio, lactate dehydrogenase, CRP, ferritin, direct bilirubin and d-dimer), presence of co-morbidities (diabetes, hypertension, asthma, coronary artery disease) and COVID-GRAM score.

Written informed consent was obtained from the patient for publication of this study. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Ventilatory variables were recorded daily. These included maximum and minimum peak end-expiratory pressure (PEEP) adjusted for mechanical ventilation, fraction of inspiratory oxygen (FiO_2), and partial pressure of oxygen (PaO_2). Peak inspiratory pressure (PINS), pressure support (PS) and PEEP were recorded 24 h prior to the development of barotrauma. In accordance with Berlin Classification, PaO_2/FIO_2 ratio was used to define acute respiratory distress syndrome (ARDS) based on degree of hypoxia [17]: mild: 200 mm Hg $< PaO_2/FIO_2 \leq$ 300 mm Hg, moderate: 100 mm Hg $< PaO_2/FIO_2 \leq$ 200 mm Hg, and severe $PaO_2/FIO_2 \leq$ 100 mm Hg. In the present study, ARDS was defined among patients with a PaO_2/FIO_2 less than 300 mm Hg, the presence of bilateral opacities on imaging, a gradual onset (7–10 days), and no existing cardiac/pulmonary pathology prior to admission [15]. Hemodynamic instability, desaturation, and increasing ventilatory parameters were the main reason(s) behind pursuing radiological imaging leading to a diagnosis of barotrauma related complications in 15.4% of our patient population.

At our institution we utilize lung-protective ventilatory strategies, with a tidal volume of 4–6 ml/kg targeting a driving pressure of 15–17 cmH2Oo and a plateau pressure not exceeding 30 cmH2O. The Fio2 was adjusted to maintain the SpO2 between 88 and 92%. In unresponsive cases, prone positioning and inhaled Nitric oxide were utilized.

Additional recorded outcomes included the length of hospital, length of ICU stay, the number of days a patient was placed on a mechanical ventilator, the date patients developed barotrauma associated pneumothorax, and the incidence of death.

All 343 patients included in the study were admitted to the ICU. Patients that were mechanically ventilated or receiving non-invasive airway support were included in the study. Identified iatrogenic pneumothorax cases and patients diagnosed with a pre-existing pneumothorax on admission were excluded.

2.2. Outcome

The primary outcome of the study was to investigate risk factors that may have led to the development of a radiologically confirmed pneumothorax/barotrauma, and the clinical prognostic implications of developing a pneumothorax in COVID-19 patients receiving care within the intensive care unit.

Whether patients received tube thoracostomy or conservative management was also documented alongside the number of days the intercostal tube remained in-situ. Invasive procedures in the thorax in the 24 h prior to the development of the pneumothorax were recorded, including central lines, bronchoscopies, removal of intercostal tubes and endotracheal intubations. The intercostal tube was removed if there was documentation of a radiographically resolved pneumothorax, the absence of an air leak, and after the paucity of negative wall suction for at least 24 h prior.

2.3. Registration

This study was registered at https://www.researchregistry.com/(unique identifying number: researchregistry6324) and work has been reported in line with the STROCSS criteria [16].

2.4. Statistical analysis

Data were analyzed using SPSS (IBM, version 25). Descriptive statistics were used to calculate mean and standard deviations for continuous data and frequency statistics were used to calculate numbers and percentages for categorical variables. Patient characteristics that developed or did not develop pneumothorax were analyses using independent *t*-test for continuous variables and chi-squared test for categorical variables. Statistical significance was set at p value less than 5%.

3. Results

Demographic, clinical and biochemical characteristics are presented in Table 1. Of the 343 patients included in the study, 285 (83.1%) were male and the mean age was 55.9 (13.5) years. Fifty-four (15.4%) patients developed barotrauma, of which 49 out of 54 patients presented with pneumothorax, and 14.8% and 3.7% was due to pneumomediastinum and pneumopericardium respectively. Of the 54 patients that developed barotrauma 52 (96.3%) patients were in ARDS (Table 2), and 5 (9.3%) received ECMO. The mean duration of developing barotrauma from admission was 10.9 (10.8) days, and mean duration of intubation prior to barotrauma development was 9.7 (11.1) days (Table 1).

Several inflammatory markers were found to be statistically different between patients that developed barotrauma compared to those that did not develop barotrauma. White blood cell count (WBC) (12.1 vs. 9.5; $p = 0.001$), neutrophil percentage (83.8 vs. 79.0; $p = 0.012$), lymphocyte percentage (10 vs 13.8; $p = 0.014$), neutrophil: lymphocyte ratio (NLR) (17.5 vs. 10; p=<0.001) and lactate dehydrogenase (LDH) (1118.9 vs. 408.0; $p = 0.002$). No statistically significant differences were found

Table 1
Demographic, Clinical and Biochemical characteristics according patients with or without Barotrauma.

	Barotrauma[a] n = 54	No Barotrauma[a] n = 289	p value[b]
Demographic			
Age, years	55.3 (15.0)	56.0 (13.3)	0.76
Gender			
Male, n (%)	42 (77.8)	243 (84.1)	0.32
Female, n (%)	12 (22.2)	46 (15.9)	
Nationality			
Kuwaiti, n (%)	18 (33.3)	92 (31.8)	0.78
Non-Kuwaiti, n (%)	36 (66.7)	197 (68.2)	
Anthropometric			
Weight, kgs	81.1 (21.0)	85.4 (20.2)	0.18
Height, m	166.0 (7.8)	167.9 (8.2)	0.17
BMI, kg/m^2	29.5 (5.3)	30.1 (6.8)	0.62
Symptoms			
Shortness of breath, n (%)	26 (48.1)	145 (50.2)	0.88
Hemoptysis, n (%)	54 (100)	289 (100)	–
Unconsciousness on admission	36 (66.7)	113 (46.0)	**0.007**
Comorbidity			
Diabetes, n (%)	20 (37.0)	123 (42.6)	0.55
hypertension, n (%)	24 (55.6)	131 (45.3)	1.00
CHD/IHD, n (%)	4 (7.4)	43 (14.9)	0.20
COPD, n (%)	1 (1.9)	4 (1.4)	0.58
Asthma, n (%)	6 (11.1)	27 (9.3)	0.62
CVD, n (%)	2 (3.7)	12 (4.2)	1.00
Hepatitis, n (%)	2 (3.7)	5 (1.7)	0.30
Cancer, n (%)	4 (7.4)	8 (2.8)	0.10
CKD, n (%)	4 (7.4)	18 (6.2)	0.76
Immunodeficiency, n (%)	1 (1.9)	2 (0.7)	0.40
History of cancer, n (%)	4 (7.4)	8 (2.8)	0.10
Outcome			
Gram score	194.1 (159.1)	159.9 (101.3)	**0.042**
Risk [c]			
Medium, n (%)	39 (11.4)	136 (47.1)	**0.006**
High, n (%)	14 (4.1)	152 (52.6)	
Death, n (%)	38 (70.4)	153 (52.9)	**0.025**
ETT, n (%)	54 (100)	225 (77.9)	**<0.001**
ECMO	5 (9.3)	19 (6.6)	0.56
Biochemical			
WBC	12.1 (7.7)	9.5 (4.8)	**0.001**
Neutrophils	83.8 (12.4)	79.0 (12.9)	**0.012**
Lymphocytes	10.0 (10.5)	13.8 (10.1)	**0.014**
NLR	17.5 (15.9)	10.0 (9.2)	**<0.001**
CRP	134.0 (111.4)	142 .4 (119.6)	0.71
Procalcitonin	4.3 (12.3)	22.2 (242.7)	0.63
Direct bilirubin	8.2 (10.3)	10.1 (29.8)	0.63
D-dimer assay	2216.2 (3918.1)	2565.6 (3191.5)	0.58
LDH	1118.9 (3513.6)	408.0 (270.2)	**0.002**
Ferritin	1413.8 (1966.4)	1082.8 (1490.1)	0.22
Length of Stay	16.4 (8.5)	20.1 (14.0)	0.11
Length of stay (ICU)	14.9 (7.8)	13.9 (12.1)	0.60
Pressure			
PEEP minimum	7.7 (2.6)	6.7 (3.8)	0.06
PEEP Maximum	14.5 (2.7)	12.5 (5.7)	**0.016**

Data are presented as means (standard deviations) for continuous variables, unless indicated. Data presented as number (percentage) for categorical variables.
Statistical Significance set at $p < 0.05$.
[a] Barotrauma associated with pneumothorax, pneumomediastinum and pneumopericardium.
[b] Independent *t*-test was carried for continuous variables. Chi-squared test was carried out for categorical variables.
[c] Only for 53/54 patients and 288/289 patients.

between CRP, procalcitonin, direct bilirubin, d-dimer assay and ferritin.

Upon admission unconsciousness was significantly higher among patients that developed and those that did not develop barotrauma (66.7% vs. 46.05; p = 0.007). All 54 patients with barotrauma were intubated and mechanically ventilated compared to 77.9% those without pneumothorax (p < 0.001), and mortality was significantly greater among those with barotrauma (70.4% vs. 52.9%; p = 0.025). No significant difference was found between barotrauma and non-barotrauma patients in receiving ECMO.

Table 2
Pressure and Volume variables specific to patients that development pneumothorax.

Barotrauma	Data
Pneumothorax, n (%)	49 (90.7)
Pneumomediastinum, n (%)	8 (14.8)
Pneumopericardium, n (%)	2 (3.7)
PEEP 24 h prior to development of barotrauma	11.7 (3.5)
Duration of intubation prior to development of barotrauma	9.7 (11.1)
Duration of barotrauma development from admission[b]	10.9 (10.8)
PaO[b] 24 h pre-trauma	92.9 (40.8)
FiO[b] 24 h pre trauma	73.4 (21.8)
PaO[b]/FiO[b] ratio 24 h	142. 0 (80.8)
ARDS, n (%)	52 (96.3)
PINS 24 h prior[a]	28.2 (8.3)
ICD duration	8.2 (9.9)
PS[a]	16.0 (6.9)
Procedure 24 h prior, n (%)	6 (11.1)

Data presented as mean (standard deviation) for continuous variables, unless indicated for categorical variables.
[a] Data available for 34/54 patients.
[b] Data available for 50/54 patients.

COVID-GRAM score was significantly higher among patients with barotrauma compared to patients that did not develop barotrauma (194.1 vs. 159.9; p = 0.042), PEEP maximum was greater among patients with barotrauma compared to those without (p = 0.016), and the incidence of death was significantly higher among patients that developed barotrauma compared to patients that did not develop barotrauma (70.4% vs. 52.9; p = 0.025).

There were no significant differences in demographic variables, presence of comorbidities, BMI, and length of hospital/ICU stay between patients with or without barotrauma.

4. Discussion

The present study focused on COVID-19 patients, analyzing the associated risk factors of barotrauma and the clinical implications with respect to their clinical course. Barotrauma complications are evident among COVID-19 patients and has been widely documented in the literature [17,18]. In this single center study, the incidence of barotrauma related complications in COVID-19 patients was 15%, which is comparable to the incidence reported by McGuinness G et al. [18].

The main indication for ICU admission in our study was patients inability to maintain oxygen saturations above 90% on high flow nasal cannula at a rate of 40 L per minute with a fraction of inspired oxygen of 100% (Fi02 100%), or the patient's inability to protect his/her airway. Several other studies have highlighted the significance of previously existing lung disease and the development of barotrauma during the delivery of invasive ventilation. In particular, conditions such as pneumonia, chronic obstructive pulmonary disease (COPD), and lung cancer are found to predispose patients to develop barotrauma [18]. Similarly, in the current study, all patients that developed barotrauma (n = 54) had underlying COVID-19 pneumonia, 11.1% were asthmatic and 1.9% had known case of COPD, In our study, 279 patients received invasive mechanical ventilation, of which 19.4% (n = 54) developed barotrauma that was radiologically confirmed consisting of either a pneumothorax, pneumomediastinum or surgical emphysema. The incidence of barotrauma in COVID-19 patients was higher to previous published studies [18].

With respect to biochemical findings, our study found that white blood count (WBC), neutrophil count, neutrophil lymphocyte ratio (NLR) and lactate dehydrogenase (LDH) were statistically greater among patients that developed barotrauma. These findings are similar to a study by Shioe et al. that reported higher levels of LDH and neutrophils

among patients infected with SARS-CoV virus, which were also found to be associated with a higher severity of lung injury. However, the study did not compare their findings to the patients that did not develop barotrauma [20]. Furthermore, we documented a statistically significant lower lymphocyte count in patients whom subsequently developed barotrauma. This finding has been found to be associated with cases of increased severity as T cells play a fundamental role in the initial and continued immune response to coronaviruses, as such T cells are unnaturally depleted [21,22].

From a clinical perspective, a Glasgow Coma Score of 8 or less requiring immediate intubation was a statistically significant variable for the development of barotrauma. This is further highlighted in our results where all 54 patients in the barotrauma group were receiving invasive mechanical ventilation in comparison to the 77.9% whom did not develop barotrauma ($p < 0.001$).

Acute respiratory distress syndrome (ARDS) has been recognized as an independent risk factor for developing barotrauma while receiving invasive ventilation. In the literature, the incidence of ARDS has been found to vary, reaching 15% in several previous studies [23–27]. In our study, of the 54 patients that developed barotrauma, 52 (96.3%) fit the criteria of ARDS within the 24 h preceding the event.

Moreover, a higher maximum PEEP was found among patients that developed barotrauma compared to the non-barotrauma patients. Although increasing PEEP values on the ventilator is part of guideline-based 'lung recruitment' maneuvers, the underlying pathophysiology of COVID-19 lung damage has been postulated to be different than typical ARDS cases [28,29]. The inability to adopt recruitment measures in COVID-19 induced ARDS lungs presents a unique situation where barotrauma is highly likely [28]. Furthermore, contrary to typical ARDS, the presence of conserved lung compliance in COVID-19 induced ARDS is distinctively different [28].

In the current study, the internally validated COVID-GRAM tool was used to assess the severity of disease and care required upon admission. A higher score was found among patients that subsequently developed barotrauma related incidents ($p = 0.042$). To our knowledge this is the first time the COVID-GRAM has been used to predict barotrauma. We reported a higher score in the patients who developed barotrauma related incidents (P value = 0.042).

In our study, the mortality was significantly greater among patients that developed barotrauma 70.4% compared to 52.9% in the non-barotrauma group ($p = 0.025$). These findings were echoed in the study by De Lassence et al. [30] Additionally, it should be noted that the mortality rate was also significantly high in the patients whom did not develop barotrauma related events; potentially a representation of a morbid cohort of patients.

5. Conclusion

In conclusion, there is a significant risk of developing barotrauma in mechanically ventilated COVID-19 patients. In our cohort of patients, we have identified specific variables that have been associated with the development of barotrauma related complications. Selecting the optimal ventilator parameters for lung recruitment while protecting against barotrauma is a delicate balance. In our study, we have reported that the development of barotrauma carries a considerable morbidity and mortality in COVID-19 patients. Further research may be required to support and re-produce these findings which may aid in establishing lung protective protocols tailored to the COVID-19 lung.

Author contribution

All authors contributed equally to the protocol, data collection, statistical analysis, and writing. Provenance and peer review Not commissioned, externally peer-reviewed.

Declaration of competing interest

All authors declare no conflict of interest.

Abbreviations

ARDS	Acute Respiratory Distress Syndrome
BMI	Body Mass Index
CHD	Coronary Heart Disease
COPD	Chronic obstructive pulmonary disease
CRP	C-reactive protein
CVD	Cerebrovascular Disease
ECMO	Extracorporeal Membrane Oxygenation
ETT	Endotracheal Tube, Mechanical ventilation
FiO2	Fraction of inspired Oxygen
ICD	Intercostal Tube Drainage
ICU	Intensive Care Unit
IHD	Ischemic Heart Disease
LDH	Lactate Dehydrogenase
NLR	Neutrophil: Lymphocyte ratio
PaO_2	Partial pressure of Oxygen
PEEP	Peak End Expiratory Pressure
PINS	Peak Inspiratory Pressure
PS	Pressure support
WBC	White Blood Count
WHO	World Health Organization

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.amsu.2021.01.089.

Please state any sources of funding for your research

Research Grant Awarded by the Kuwait Foundation for Advancement of Science (KFAS). Grant number: Cor-prop- 35.

Ethical approval

Ethical approval for the study was granted by the Ministry of Health Ethical Review Board in Kuwait. Reference number 1402/2020 on March 29, 2020.

Consent

Written informed consent was obtained from all patients included in the study.

Registration of research studies

1. Name of the registry: https://www.researchregistry.com/
2. Unique Identifying number or registration ID: researchregistry6324.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.researchregistry.com/browse-the-registry#user-researchregistry/registerresearchdetails/5fc7a9f2e6b001001be74d5e/

Guarantor

Salman Al-Sabah salman.k.alsabah@gmail.com.

References

[1] World Health Organization, Director-General's Remarks at the Media Briefing on 2019-nCoV on 11 February, 2020. Accessed on February 12, 2020, https://www.

who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020.
[2] J.F. Chan, S. Yuan, K.H. Kok, et al., A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster, Lancet 395 (2020) 514.
[3] K.L. Bajema, A.M. Oster, O.L. McGovern, et al., Persons evaluated for 2019 novel coronavirus - United States, january 2020, MMWR Morb. Mortal. Wkly. Rep. 69 (2020) 166.
[4] C. Huang, Y. Wang, X. Li, et al., Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China, Lancet 395 (2020) 497.
[5] N. Chen, M. Zhou, X. Dong, et al., Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study, Lancet 395 (2020) 507.
[6] D. Wang, B. Hu, C. Hu, et al., Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in wuhan, China, J. Am. Med. Assoc. 323 (11) (2020) 1061–1069.
[7] K. Liu, Y.Y. Fang, Y. Deng, et al., Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province, Chin. Med. J. 133 (2020) 1025.
[8] X. Yang, Y. Yu, J. Xu, et al., Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study, Lancet Respir Med 8 (5) (2020) 475–481.
[9] X. Yang, Y. Yu, J. Xu, et al., Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study, Lancet (2020).
[10] Z. Wu, J.M. McGoogan, Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese center for disease control and prevention, J. Am. Med. Assoc. 323 (13) (2020) 1239–1242.
[11] C.M. Petrilli, S.A. Jones, J. Yang, et al., Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study, BMJ 369 (2020) m1966.
[12] F. Zhou, T. Yu, R. Du, et al., Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study, Lancet 395 (2020) 1054–1112.
[13] J. Lighter, M. Phillips, S. Hochman, et al., Obesity in patients younger than 60 years is a risk factor for Covid-19 hospital admission, Clin. Infect. Dis. 71 (15) (2020 Jul 28) 896–897.
[14] W. Liang, H. Liang, L. Ou, B. Chen, A. Chen, C. Li, Y. Li, W. Guan, L. Sang, J. Lu, Y. Xu, Development and validation of a clinical risk score to predict the occurrence of critical illness in hospitalized patients with COVID-19, JAMA Internal Medicine 180 (8) (2020 May 12) 1081–1089.
[15] A.D. Force, V.M. Ranieri, G.D. Rubenfeld, B.T. Thompson, N.D. Ferguson, E. Caldwell, Acute respiratory distress syndrome, Jama 307 (23) (2012 Jun 20) 2526–2533.
[16] R. Agha, A. Abdall-Razak, E. Crossley, N. Dowlut, C. Iosifidis, G. Mathew, M. Bashashati, F.H. Millham, D.P. Orgill, A. Noureldin, I.J. Nixon, STROCSS 2019 Guideline: strengthening the reporting of cohort studies in surgery, Int. J. Surg. 72 (2019 Dec 1) 156–165.
[17] M. Abdallat, M. Khalil, G. Al-Awwa, R. Kothuru, C. La Punzina, Barotrauma in COVID-19 patients, Journal of Lung Health and Diseases 4 (2) (2020 Jun 26).
[18] G. McGuinness, C. Zhan, N. Rosenberg, L. Azour, M. Wickstrom, D.M. Mason, K. M. Thomas, W.H. Moore, High incidence of barotrauma in patients with COVID-19 infection on invasive mechanical ventilation, Radiology (2020 Jul 2) 202352.
[20] A.D. Sihoe, R.H. Wong, A.T. Lee, L.S. Lau, N.Y. Leung, K.I. Law, A.P. Yim, Severe acute respiratory syndrome complicated by spontaneous pneumothorax, Chest 125 (6) (2004 Jun 1) 2345–2351.
[21] H.L. Janice Oh, S. Ken-En Gan, A. Bertoletti, Y.J. Tan, Understanding the T cell immune response in SARS coronavirus infection, Emerg. Microb. Infect. 1 (1) (2012 Jul 1) 1–6.
[22] H.S. Shin, Y. Kim, G. Kim, J.Y. Lee, I. Jeong, J.S. Joh, H. Kim, E. Chang, S.Y. Sim, J. S. Park, D.G. Lim, Immune responses to Middle East respiratory syndrome coronavirus during the acute and convalescent phases of human infection, Clin. Infect. Dis. 68 (6) (2019 Mar 5) 984–992.
[23] R.B. Gammon, M.S. Shin, S.E. Buchalter, Pulmonary barotrauma in mechanical ventilation: patterns and risk factors, Chest 102 (2) (1992 Aug 1) 568–572.
[24] M.D. Eisner, B.T. Thompson, D. Schoenfeld, A. Anzueto, M.A. Matthay, Acute Respiratory Distress Syndrome Network. Airway pressures and early barotrauma in patients with acute lung injury and acute respiratory distress syndrome, Am. J. Respir. Crit. Care Med. 165 (7) (2002 Apr 1) 978–982.
[25] R.B. Gammon, M.S. Shin, R.H. Groves Jr., J.M. Hardin, C. Hsu, S.E. Buchalter, Clinical risk factors for pulmonary barotrauma: a multivariate analysis, Am. J. Respir. Crit. Care Med. 152 (4) (1995 Oct) 1235–1240.
[26] J.G. Weg, A. Anzueto, R.A. Balk, H.P. Wiedemann, E.N. Pattishall, M.A. Schork, L. A. Wagner, The relation of pneumothorax and other air leaks to mortality in the acute respiratory distress syndrome, N. Engl. J. Med. 338 (6) (1998 Feb 5) 341–346.
[27] Acute Respiratory Distress Syndrome Network, Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome, N. Engl. J. Med. 342 (18) (2000 May 4) 1301–1308.
[28] C. Pan, L. Chen, C. Lu, W. Zhang, J.A. Xia, M.C. Sklar, B. Du, L. Brochard, H. Qiu, Lung recruitability in COVID-19–associated acute respiratory distress syndrome: a single-center observational study, Am. J. Respir. Crit. Care Med. 201 (10) (2020 May 15) 1294–1297.
[29] L. Gattinoni, S. Coppola, M. Cressoni, M. Busana, S. Rossi, D. Chiumello, Covid-19 does not lead to a “typical” acute respiratory distress syndrome, Am. J. Respir. Crit. Care Med. 201 (10) (2020 May 15) 1299–1330.
[30] A. de Lassence, J.F. Timsit, M. Tafflet, E. Azoulay, S. Jamali, F. Vincent, Y. Cohen, M. Garrouste-Orgeas, C. Alberti, D. Dreyfuss, OUTCOMEREA® Study Group, Pneumothorax in the intensive care unit: incidence, risk factors, and outcome, The Journal of the American Society of Anesthesiologists 104 (1) (2006 Jan 1) 5–13.